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10/550,155	10/04/2006	Kevin Gray	D1990-1N	1058

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VERENIUM CORPORATION
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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
10/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,155	GRAY ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52,72,82,83,86,166 and 191* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/06; 11/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,25,29,32-34,37,40,42,44,46,48,49,51,52,72,82,83,86,87,89,91,94,96,103,110,114,124,129,160,162,166,169,170,172-180,182,184,185,189-191,207,209,213,216 and 217.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,25,29,32-34,37,40,42,44,48,49,51,89,91,94,96,103,110,114,124,129,160,162,169,172-180,182,184,185,187,189,190,207,209,213,216 and 217.

DETAILED ACTION

This application is a 371 of PCT/US04/08541.

The preliminary amendment filed on 6/6/2008 amending claims 1, 25, 52, and 207 is acknowledged. Claims 2-24, 26-28, 30-31, 35-36, 38-39, 41, 43, 45, 47, 50, 53-71, 73-81, 84-85, 88, 90, 92-93, 95, 97-102, 104-109, 111-113, 115-123, 125-128, 130-159, 161, 163-165, 167-168, 171, 181, 183, 186, 188, 192-206, 208, 210-212, 214-215, and 218 remain canceled.

Claims 1, 25, 29, 32-34, 37, 40, 42, 44, 46, 48-49, 51-52, 72, 82-83, 86-87, 89, 91, 94, 96, 103, 110, 114, 124, 129, 160, 162, 166, 169-170, 172-180, 182, 184-185, 189-191, 207, 209, 213, 216-217 are currently pending in the instant application.

Election/Restriction

Applicant's election with traverse of Group VII, claims 52, 72, 82, 83, 86, 166, 191, 209, and 213, drawn to a recombinant polypeptide with a glucosidase activity or a protein preparation or a homodimer or a heterodimer polypeptide, a chimeric protein, a composition, a pharmaceutical composition or a detergent composition, and a protein of SEQ ID NO: 10 or a nucleic acid encoding SEQ ID NO: 10 in the response filed on 6/16/2008 is acknowledged.

The traversal is on the ground(s) that after entry of the amendment, all pending claims in this application satisfy PCT Rule 13.2 in that they will share the novel inventive concept based on the exemplary SEQ ID NO: 10 encoded by the genus of

polynucleotides based on the exemplary of SEQ ID NO: 9, which is not persuasive because claim 52 recites a polypeptide which is 75% sequence identical to SEQ ID NO: 10 over the region of 100 amino acid residues --- or subsequence thereof. Cao et al. (US2003/233675-A1, publication 12/18/2003, claimed priority of 60/360,039 filed on 2/21/2002) teach a polypeptide, which is 83% identical to amino acid position 79 to 180 of SEQ ID NO: 10, which is within the scope of the claim. Therefore, a polypeptide, which is 75% sequence identical to SEQ ID NO: 10 over the region of 100 amino acid residues --- or subsequence thereof, does not make contribution over the prior art and lack unity of invention. Besides, the PCT does not provide for multiple products or methods within a single application, therefore, unity of invention is lacking with regard to Groups I-XXXII ; see 37 CFR 1.475. 37 CFR 1.475 (d) also states: If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) **1.47(c).** Furthermore, the search is not limited to only patent database but also includes large non-patent databases. Searching Groups I - XXXII and analyzing the vast search results from both patent and non-patent databases imposes a serious burden on the Examiner. Restriction is clearly permissible even among related inventions as defined in MPEP 808, and 35 U.S.C. 121 allows restriction of inventions, which are independent or distinct. After careful review of the restriction requirement, the Examiner finds that claims 209 and 213 should have grouped in Group XXXII, with

claim 207 because claims 207, 209 and 213 encompass a chimeric protein comprising signal peptide and optionally a heterologous protein.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 25, 29, 32-34, 37, 40, 42, 44, 48-49, 51, 89, 91, 94, 96, 103, 110, 114, 124, 129, 160, 162, 169, 172-180, 182, 184-185, 187, 189-190, 207, 209, 213, 216 and 217 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 52, 72, 82, 83, 86, 87, 166, and 191 are under consideration and are present for examination.

Applicants request for rejoinder is noted, however, claimed product is not allowable at this time. When claimed product would be allowable; rejoinder request would be evaluated at that time.

Priority

Acknowledgement is made of applicants claim for international application PCT/US04/08541filed on 3/18/2004, which claim for domestic priority under 35 USC 119(e) to provisional application 60/456,972 filed on 3/20/2003.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 11/08/06 and 2/6/06 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97.

Accordingly, the information disclosure statements are considered by the examiner. The signed copies of IDSs are enclosed herewith.

Drawings

Drawings submitted on 9/20/2005 are accepted by the Examiner.

Objections to Abstract

The abstract of the disclosure is objected to because, Abstract should be on a separate sheet of paper. Appropriate correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 87 is objected to as encompassing non-elected subject matter, i.e. claim continue to recites "nucleic acid". Appropriate correction is required.

Claims 52 and 87 are objected to as depending from non-elected claim. Appropriate correction is required.

Claim 191 is objected to as depending from non-elected claim. Appropriate correction is required.

Claim 52 is objected to because of the recitation ".alpha.", which should be "alpha". Appropriate correction is required.

Claim 52 is objected to because of the recitation "95° C.", which should be "95° C". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 52 is indefinite in the recitation "at least about 100 ----" which is ambiguous and confusing. It is unclear whether applicant meant "at least 100 --- residues" or "about 100 ---residues". However, "about 100 --- residues" is unclear and vague, as it is not clearly stated in the specification about what is the scope of "about 100 ---residues" mean? In addition, the combination of "at least about 100 --- residues" is ambiguous and confusing. Accordingly, claims 72, 82, 83, 86, 166, and 191 are also rejected, as they depend on claim 52.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and

Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 52 recites the broad recitation 75%, and the claim also recites 76%, 77%, 78%, 79%, 80%, 81% --- 90% ----, 95% and 97%, which is the narrower statement of the range/limitation, wherein this claim also recites broad to narrow ranges of lengths over which the homology must occur.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 52 is indefinite in the recitation of multiple "optionally" in the context of substrate, optimum temperature, specific activity or pH range, which is confusing. It is unclear as to what limitation is necessary for the claimed invention. Accordingly, claims 72, 82, 83, 86, 166, and 191 are also rejected, as they depend on claim 52.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 52 is

indefinite in the recitation of "pH 4.5, 5, 8.0, 8.5, 9, 10, 10 or 10.5" because it is not clear as to which pH is being recited necessary for the claimed invention.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 52 recites the broad recitation 37oC to 95oC and the claim also recites 55oC to 85oC, 70oC to 95oC, and 90oC to 95oC which is the narrower statement of the range/limitation. Similarly, As such, it is unclear to which temperature range the phrase refers.

Claims 83 and 86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. Claims 83 and 86 are confusing in the recitation of "A heterodimer" or "homodimer" as the remainder of the claims and the specification suggest that applicants intend these claims to encompass fusion proteins (i.e., covalently bound proteins) of the polypeptide of Claim 52 yet the terms heterodimer and homodimer in the art would mean non-covalently bound association of two polypeptide chains (either two different chains or two identical chains respectively). As such the meaning of these terms is confusing. It is suggested that the claims be amended to recite a fusion polypeptide.

Claim 87 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 87 is indefinite in the recitation of "polypeptide comprises the nucleic acid sequence", which is ambiguous and confusing. A protein cannot have a nucleotide sequence as is claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 52, 72, 82, 83, 86, 166, and 191 are directed to a genus of a polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence or comprising a signal sequence, which is either endogenous or heterologous signal sequence or a protein preparation comprises a liquid, a solid or a gel, including homodimer or immobilized, a detergent composition, or a pharmaceutical composition. As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification teaches the structure of only a single representative species of such proteins. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding the polypeptide having glucosidase activity. Given this lack of description of representative species encompassed by the genus of proteins in the

claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide of SEQ ID NO: 10 encoded by SEQ ID NO: 9 having glucosidase activity, wherein the polypeptide comprising a catalytic domain, or a protein preparation comprises a liquid, a solid or a gel, including homodimer or immobilized, a detergent composition, or a pharmaceutical composition comprising SEQ ID NO: 10, does not reasonably provide enablement for any polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence or comprising a signal sequence, which is either endogenous or heterologous signal sequence or a protein preparation comprises a liquid, a solid or a gel, including any homodimer or any immobilized protein, a detergent composition comprising said polypeptide, or a pharmaceutical composition comprising said polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731,737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows:

(1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claims. The factors, which have, lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed below:

The breadth of the claims:

Claims 52, 72, 82, 83, 86, 166, and 191 are so broad as to encompass any polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence or comprising a signal sequence, which is either endogenous or heterologous signal sequence or a protein preparation comprises a liquid, a solid or a gel, including any homodimer or any immobilized protein, a detergent composition comprising said polypeptide, or a pharmaceutical composition comprising said polypeptide.

The scope of the claim is also not commensurate with the enablement provided by the disclosure with regard to the extremely large number of glucosidase proteins including mutants and variants broadly encompassed by the claims. In the instant case

the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single protein of SEQ ID NO: 10 and compositions (detergent or pharmaceutical) comprising said SEQ ID NO: 10.

The amount of direction or guidance presented and the existence of working examples:

The specification discloses a polypeptide of SEQ ID NO: 10 encoded by SEQ ID NO: 9 having glucosidase activity, wherein the polypeptide comprising a catalytic domain, or a protein preparation comprises a liquid, a solid or a gel, including homodimer or immobilized, a detergent composition, or a pharmaceutical composition comprising SEQ ID NO: 10. However, the specification fails to provide any clue as to the structural elements required in any polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, or a protein preparation comprises a liquid, a solid or a gel, including any homodimer or any immobilized protein, a detergent composition comprising said polypeptide, a pharmaceutical composition or a chimeric fusion protein comprising said polypeptide or which are the structural elements in a polypeptide having 6-25% non-identity to SEQ ID NO: 10 known in the art that are essential for any protein to display glucosidase enzymatic activity. No correlation between structure and function has been presented.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art:

The amino acid sequence of a protein determines its structural and functional

properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, the protein which is 75% identical to SEQ ID NO: 10 i.e. 25% comprises mutants, and variants. The art clearly teaches the high level of unpredictability with regard to the effect of structural changes in a protein's activity when no guidance/knowledge as to which amino acids are required for activity has been provided. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. Whisstock et al. (2003) teach that prediction of protein function from sequence and structure is a difficult problem because homologous proteins often have different functions (see abstract). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. Similarly, at the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (1991 teach that (1) protein engineers are

frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing de novo stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (1999) and Seffernick et al. (2001), where it is shown that even small amino acid changes result in enzymatic activity changes.

The quantity of experimentation required practicing the claimed invention based on the teachings of the specification:

While methods of generating or isolating variants of a polypeptide were well known in the art at the time of invention, it is not routine in the art to screen by trial and error process for (1) all or any protein which is 75% identical to SEQ ID NO: 10, (2) an essentially infinite number of mutations of any polypeptide of SEQ ID NO: 10 amino acid sequence. The amino acids modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The specification does not support the broad scope of the claims which encompass any polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 or a subsequence thereof, or a protein preparation comprises a liquid, a solid or a gel, including any homodimer or any immobilized protein, a detergent composition comprising said polypeptide, or a pharmaceutical composition comprising said polypeptide because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting glucosidase enzyme activity; (B) the general tolerance of glucosidase polypeptides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in glucosidase polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polypeptide, which is 75-94% sequence identical to SEQ ID NO: 10 or a subsequence thereof, or a protein preparation comprises a liquid, a solid or a gel, including any homodimer or any immobilized protein, a detergent composition comprising said polypeptide, or a pharmaceutical composition comprising said polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a polypeptide having the desired biological characteristics is unpredictable and the experimentation left to

those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 52, and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Willis et al. (Novel Sinorhizobium meliloti operon encodes an alpha-glucosidase and a periplasmic-binding-protein-dependent transport system for alpha-glucosides, J Bacteriol. 1999 Jul;181(14):4176-84). Instant claims are directed to a polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence or comprising a signal sequence, or a homodimer comprising said protein liquid, and a pharmaceutical composition comprising said protein.

Willis et al. teach a novel Sinorhizobium meliloti operon encodes an alpha-glucosidase, which is 55% identical to SEQ ID NO: 10 of the instant application having alpha-glucosidase activity, wherein said protein is 76% identical to amino acid position 79-182 of SEQ ID NO: 10 (see sequence alignment) and having no signal sequence. Therefore, Willis et al. anticipate claims 52, and 72 of the instant application as written.

Claims 52, 72, 82 and 191 are rejected under 35 U.S.C. 102(b) as being anticipated by Cao et al. (US PGPUB 2003/233675-A1, publication 12/18/2003, claim priority of 60/360039 filed on 2/21/2002). Instant claims are directed to a polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence or comprising a signal sequence, a protein preparation comprises a liquid and a pharmaceutical composition comprising said protein.

Cao et al. teach a novel bacterial alpha-glucosidase [0043], which is 54% identical to SEQ ID NO: 10 of the instant application having alpha-glucosidase activity, wherein said protein is 78% identical to amino acid position 61-160 of SEQ ID NO: 10 (see sequence alignment) and having no signal sequence. Cao et al. also teach purification of the protein [0081], i.e. present in solution. Cao et al. further teach that said protein can be used in pharmaceutical preparation [0048]. Cao et al. further teach that said protein is heat tolerant [0040]. Therefore, Cao et al. anticipate claims 52, 72, 82, 86, and 191 of the instant application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 83, and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al. (US PGPUB 2003/233675-A1, publication 12/18/2003, claim priority of 60/360039 filed on 2/21/2002) as applied to claims 52, 72, 82, 86, and 191 above and further in view of Stempfer et al. (A fusion protein designed for noncovalent immobilization: stability, enzymatic activity, and use in an enzyme reactor, Nature Biotechnol. 1996 Apr;14(4):481-4). Instant claims are directed to a polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof, wherein the polypeptide lacking signal sequence, a heterodimer fusion protein comprising an epitope or tag and immobilization of said polypeptide with polymer.

Cao et al. teach a novel bacterial alpha-glucosidase [0043], which is 54% identical to SEQ ID NO: 10 of the instant application having alpha-glucosidase activity,

wherein said protein is 78% identical to amino acid position 61-160 of SEQ ID NO: 10 (see sequence alignment) and having no signal sequence. Cao et al. also teach purification of the protein [0081], i.e. present in solution. Cao et al. teach that said protein can be used in pharmaceutical preparation [0048]. Cao et al. further teach that said protein is heat tolerant [0040]. Cao et al. do not teach a fusion protein with an epitope or tag or immobilization of the said protein with a polymer.

Stempfer et al. teach a fusion protein designed for noncovalent immobilization: stability, enzymatic activity, and use in an enzyme reactor, wherein said fusion protein is alpha-glucosidase containing at its C-terminus a polycationic hexa-arginine fusion peptide as tag. This fusion protein can be directly adsorbed from crude cell extracts on polyanionic matrices in a specific, oriented fashion (abstract).

Stempfer et al. clearly teach a fusion protein with an epitope or tag and immobilization of the said protein with a polymer.

By combining the teachings of Cao et al. and Stempfer et al., it would have been obvious to one to ordinary skill in the art at the time of the invention was made using the polypeptide of Cao et al. to make a fusion protein comprising an epitope or tag for immobilization as taught by Stempfer et al. to adsorbed on a matrices.

One of ordinary skill in the art would have been motivated to noncovalent immobilization of said protein by polyionic interactions in order to increase the stability of the fusion protein, which is not affected by pH-, urea-, or thermal-denaturation.

One of ordinary skill in the art would have a reasonable expectation of success because Stempfer et al. could successfully make a fusion protein and immobilized on the surface of a polyanionic matrices.

Therefore, claims 83, 87 and 209 would have been prima *facie* obvious to use one of ordinary skill in the art.

Claim 166 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cao et al. (US PGPUB 2003/233675-A1, publication 12/18/2003, claim priority of 60/360039 filed on 2/21/2002) as applied to claims 52, 72, 82, 86, and 191 above and in view of Outtrup et al. (US 6309871, issued on 10/30/2001, see IDS).

Instant claims are directed to a detergent composition comprising a polypeptide having glucosidase activity, which is 75-94% sequence identical to SEQ ID NO: 10 over a region of 100-500 amino acid residues or the full length of SEQ ID NO: 10 or a subsequence thereof.

Cao et al. teach a novel bacterial alpha-glucosidase [0043], which is 54% identical to SEQ ID NO: 10 of the instant application having alpha-glucosidase activity, wherein said protein is 78% identical to amino acid position 61-160 of SEQ ID NO: 10 (see sequence alignment) and having no signal sequence. Cao et al. also teach purification of the protein [0081], i.e. present in solution. Cao et al. teach that said protein can be used in pharmaceutical preparation [0048]. Cao et al. further teach that said protein is heat tolerant [0040]. Cao et al. do not teach a detergent composition comprising said polypeptide.

Outtrup et al. teach a detergent composition comprising a polypeptide having alpha-amylase activity (a glucosidase) fusion protein designed for noncovalent immobilization: stability, enzymatic activity, and use in an enzyme reactor, wherein said fusion protein is alpha-glucosidase containing at its C-terminus a polycationic hexa-arginine fusion peptide as tag. This fusion protein can be directly adsorbed from crude cell extracts on polyanionic matrices in a specific, oriented fashion. Outtrup et al. further teach fusion protein comprising signal peptide (p11-12, paragraph 6).

Outtrup et al. clearly teach a fusion protein and a detergent composition comprising said protein.

By combining the teachings of Cao et al. and Outtrup et al., it would have been obvious to one to ordinary skill in the art at the time of the invention was made to use the polypeptide of Cao et al. for making a detergent composition comprising said polypeptide as taught by Outtrup et al.

One of ordinary skill in the art would have been motivated to make a detergent composition comprising said polypeptide because of heat tolerant properties of the polypeptide as taught by Cao et al. to use in washing or laundry industry for economical purpose.

One of ordinary skill in the art would have a reasonable expectation of success because Outtrup et al. could successfully use a polypeptide in detergent composition.

Therefore, claim 166 would have been prima *facie* obvious to use one of ordinary skill in the art.

Conclusion

Status of the claims:

Claims 1, 25, 29, 32-34, 37, 40, 42, 44, 46, 48-49, 51-52, 72, 82-83, 86-87, 89, 91, 94, 96, 103, 110, 114, 124, 129, 160, 162, 166, 169-170, 172-180, 182, 184-185, 189-191, 207, 209, 213, 216-217 are currently pending.

Claims 1, 25, 29, 32-34, 37, 40, 42, 44, 48-49, 51, 89, 91, 94, 96, 103, 110, 114, 124, 129, 160, 162, 169, 172-180, 182, 184-185, 187, 189-190, 207, 209, 213, 216 and 217 are withdrawn.

Claims 52, 72, 82, 83, 86, 166, and 191 are rejected.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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